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Norman H Stepno Burns Doane Swerker & Mathis			WHITEMAN, BRIAN A	
PO Box 1404			ART UNIT	PAPER NUMBER
Alexandria, VA 22313-1404			1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

## Application No. Applicant(s) 09/762,573 REGULIER ET AL. Office Action Summary Examiner **Art Unit** Brian Whiteman 1635 -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --Period for Reply A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION. Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication. If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely. If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication. Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b). **Status** 1) Responsive to communication(s) filed on 17 May 2004. 2a) This action is **FINAL**. 2b) This action is non-final. 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11, 453 O.G. 213. **Disposition of Claims** 4) $\boxtimes$ Claim(s) 1,7,11-15,19,25-40 is/are pending in the application. 4a) Of the above claim(s) is/are withdrawn from consideration. 5) Claim(s) \_\_\_\_\_ is/are allowed. 6) Claim(s) <u>1,7,11-15,19,25-40</u> is/are rejected. 7) Claim(s) \_\_\_\_\_ is/are objected to. 8) Claim(s) are subject to restriction and/or election requirement. **Application Papers** 9) The specification is objected to by the Examiner. 10) The drawing(s) filed on is/are: a) accepted or b) objected to by the Examiner. Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a). Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d). 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152. Priority under 35 U.S.C. § 119 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f). a) ☐ All b) ☐ Some \* c) ☐ None of: 1. Certified copies of the priority documents have been received. 2. Certified copies of the priority documents have been received in Application No. \_\_\_ 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)). \* See the attached detailed Office action for a list of the certified copies not received.

MILLAUI	imeni(s)

1) 🔼	Notice of References Cited (PTO-892)	
2) 🔲	Notice of Draftsperson's Patent Drawing	Review (I

Paper No(s)/Mail Date \_\_\_\_\_.

3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)

4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. \_\_\_\_\_.

5) Notice of Informal Patent Application (PTO-152)

6) Other: \_\_\_\_.

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#### **DETAILED ACTION**

### Non-Final Rejection

Claims 1, 7, 11-15, 19, and 25-40 are pending.

Applicant's traversal, the cancellation of claims 20 and 24, the amendment to claims 1, 14, and 19, and the addition of claims 33-40 in paper filed on 5/17/04 is acknowledged and considered.

## Claim Objections

Claim 33 is objected to because of the following informalities: there should be a space between the terms "MIP1a" and "or" on line 5. Appropriate correction is required.

#### Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 33-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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New claims 33-40 filed on 5/17/04 introduce new subject matter into the application. The application and the originally filed claims as a whole are directed to a composition comprising: (i) a nucleic acid sequence encoding all or part of an MIP chemokine, (ii) at least one nucleic acid sequence encoding IL-2, said nucleic acid sequence being placed under the control of elements required for the expression in a host cell of said mammal and using the composition to treat a proliferative disorder in a patient.

The original specification and claims do not disclose the limitation, "wherein the IL-2 and MIP chemokine work together synergistically to inhibit the growth or cause the rejection of a tumor in said patient when compared to the anti-tumor response in said patient administered with a composition comprising a vector comprising only the nucleic acid sequence (i) or the nucleic acid sequence (ii)" in the new claims. The pages cited for support of the new claims do not provide support for the new claims. See Pages 29-32 in the examples and Figures 1-6. The specification recites, "We have now identified novel cytotoxic compositions in which the various constituents are chosen so to obtain a synergistic effect of their respective activities and improved properties of said constituents" (Page 3, lines 17-20). However, the specification does not describe what is a synergistic effect and does not specifically point out what cytotoxic composition produces a synergistic effect. In addition, the working examples do not disclose a composition comprising a nucleic acid sequence encoding an MIP chemokine and a nucleic acid sequence encoding IL-2, wherein the IL-2 and MIP chemokine work together synergistically compared to a composition comprising the a vector comprising only the nucleic acid sequence encoding IL-1 or a vector comprising only the nucleic acid sequence encoding MIP. It is apparent that the applicants at the time the invention was made did not intend or contemplate the

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claimed invention as part of the disclosure of their invention. There is no evidence in the specification that the applicants were possession of the claimed method, where IL-2 and MIP chemokine working together synergistically, at the time the application was filed.

Applicant's arguments filed 5/17/04 have been fully considered but they are not persuasive.

With respect to applicants' arguments that Example 2 shows that anti-tumor protection provided by compositions associating the action of IL-2 and a MIP chemokine in three different tumor models as compared to the anti-tumor effect observed with individual vector encoding IL-2, MIP-1α or MIP-1β, the argument is not found persuasive because the rejection is based on the specification not providing description of a synergistic method for treating a proliferative disorder in a patient and the rejection is not based on whether the compositions show anti-tumor protection. Furthermore, it is not apparent how the compositions show anti-tumor protection if tumors are already present on the animal. The specification does not disclose that the compositions provide anti-tumor protection. In addition, the specification and the prior art do not disclose a nexus between anti-tumor protection and an anti-tumor effect. The term "anti-tumor effect" is a broad term that encompasses improved increase in survival rate, decrease tumor volume and anti-tumor protection.

With respect to applicants' argument that Figures 1 and 2 provide support for the new claims, the argument is not found persuasive because the survival rate in Figure 2 for IL-2 is longer than MIP1alpha and IL-2 combined. Figure 2 does not display a synergistic combination using MIP1alpha and IL-2. Furthermore, the Figures display results using a construct for MIP1a, IL2, and MIP1a+IL2, but no result for MIP1b+IL-2.

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In addition, with respect to applicants' argument that Figures 3 and 4 provide support for the new claims, the argument is not found persuasive because the Figures display that IL-2 compared MIP1alpha + IL-2 have a similar decrease in tumor burden and the combination does not display a synergistic combination. With respect to applicants' argument that Figure 4 provides support for the new claims because 36% of mice implanted with Renca tumors were tumor-free at least 100 days after intratumoral injection of an adenoviral vector expressing both IL-2 and MIP1-beta compared to an adenoviral vector expressing MIP1beta or IL-2, the argument is not found persuasive because IL-2 and MIPbeta + IL-2 have similar results. The assertion that the mice were tumor-free is not supported by the specification because the specification does not disclose that the mice exposed to MIPbeta+IL-2 were tumor free at least 100 days. The specification does disclose that 36% of mice from the group survived for 100 days. In addition, it is not apparent how a mouse can be tumor-free for 100 days if the same mouse has a tumor for those 100 days.

With respect to applicants' argument that Figures 5 and 6 provide support for the new claims, the argument is not found persuasive because the Figures do not display a composition comprising a nucleic acid sequence encoding an MIP chemokine and a nucleic acid sequence encoding IL-2, wherein the IL-2 and MIP chemokine work together synergistically compared to a composition comprising the a vector comprising only the nucleic acid sequence encoding IL-1 or a vector comprising only the nucleic acid sequence encoding MIP. For this reason, the applicants do not provide any evidence of record that one skilled in the can correlate that these figures provide support for the claimed method. Furthermore, the applicants' assertion that "As shown in Figure 6, the anti-tumor protection provided by the adenoviral vector co-expressing IL-

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2 and MIP1alpha is even more pronounced in the P815 model, because 67% of the treated mice implanted with P815 tumors were tumor free at least 90 days after intratumoral injection" is not supported by any evidence of record because Figure 6 is directed to survival rate. The specification does not disclose that Figure 6 displays that the treated mice were tumor free. The specification discloses that 67% of the mouse from this experimental group survived.

### Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

- 1. Determining the scope and contents of the prior art.
- 2. Ascertaining the differences between the prior art and the claims at issue.
- 3. Resolving the level of ordinary skill in the pertinent art.
- 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

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invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 7, 11-15, 19, 26, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boursnell et al. (US Patent 6,287,557) taken with Hobart et al. (US Patent 5,147,055) and LaFace (US 6,649,158) and Song et al., (J.Exp. Med., 186:1247-1256, 1997).

Boursnell teaches virus vectors encoding nucleotide sequences expressing immunomodulating proteins including cytokines and chemokines and combinations thereof (col. 6, lines 55-67), such as IL-2 and MIP1B (col. 7, lines 1-11) for cancer immunotherapy, wherein each of the sequences are placed under control of a known viral promoter or a mammalian specific promoter (col. 9, lines 45-51). Boursnell further teaches making and using a vector comprising two or more nucleotide sequences or a mixture of two vectors containing at least one gene encoding a different immunomodulator product (col. 8, lines 50-55). Furthermore, Boursnell teaches a method of using the vector for cancer immunotherapy in an animal by direct or indirect administration (col. 11, lines 8-67). The vector can be a mutant DNA or RNA virus, e.g., adenovirus, poxvirus (col. 5, lines 49-55). The vectors used in the method taught by Boursnell are in pharmaceutically acceptable formulas. However, Boursnell does not specifically teach a composition comprising a nucleotide sequence encoding IL-2 and a nucleotide sequence encoding a MIP1-beta. In addition, Boursnell does not specifically teach using a composition comprising at least two nucleotide sequences encoding IL-2 and a nucleotide sequence encoding a MIP1-beta. In addition, Boursnell does not specifically teach inserting the nucleic acid sequences into either the same vector or a distinct vector.

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However, at the time the invention was made, Hobart teaches a method of treating a solid tumor in an animal comprising introducing a vector comprising IL-2 into the solid tumors (col. 4, lines 33-41, col. 4, line 66- col. 5, and col. 33, line 33 to col. 36, line 37).

In addition, at the time the invention was made, LaFace teaches that MIP-1.beta. is a dendritic cell chemoattractant (DCC) that induces chemotaxis of mature dendritic cells (columns 11-12). Song teaches that dendritic cells are potent antigen-presenting cells that play a critical role in the initiation of an anti-tumor immune response (page 1247).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Boursnell taken with Hobart and LaFace and Song to make and use a composition comprising a nucleotide sequence encoding IL-2 and a nucleotide sequence encoding an MIP1-beta. One of ordinary skill in the art would have been motivated to combine the teachings because a composition comprising a nucleotide sequence encoding IL-2 and a nucleotide sequence encoding MIP1β were well known to one of ordinary skill in the art for treating tumors in an animal. Therefore, is would been obvious to one of ordinary skill in the art to make the composition.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Boursnell taken with Hobart and LaFace and Song to make and use a composition comprising at least two nucleotide sequences encoding IL-2 and a nucleotide sequence encoding a MIP1β. One of ordinary skill in the art would have been motivated to combine the teachings to increase the reduction of tumor cells by using two nucleotide sequences encoding IL-2.

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It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Boursnell taken with Hobart and LaFace and Song to insert a nucleotide sequence encoding IL-2 and a nucleotide sequence encoding MIP1β into the same vector. One of ordinary skill in the art would have been motivated to insert both sequences into the same vector to simplify delivering the sequences to a cell and because Boursnell teaches that it was routine to one of ordinary skill in the art to use one vector comprising two different nucleotide sequences.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Boursnell taken with Hobart and LaFace and Song to insert a nucleotide sequence encoding IL-2 and a nucleotide sequence encoding MIP1β into distinct vectors. One of ordinary skill in the art would have been motivated to insert both sequences into different vectors because Boursnell teaches that it was routine to one of ordinary skill in the art to use two different vectors comprising two different nucleotide sequences.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Boursnell taken with Hobart and LaFace and Song to make a composition comprising a nucleotide sequence encoding IL-2 and a nucleotide sequence encoding a MIP1β, wherein the composition is inserted into a recombinant adenovirus vector. One of ordinary skill in the art would have been motivated to combine the teachings because recombinant adenoviral vectors comprising an anti-tumor gene were well known to one of ordinary skill in the art for reducing tumors in an animal. Therefore, is would been obvious to one of ordinary skill in the art to make the adenoviral vector.

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It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Boursnell taken with Hobart and LaFace and Song to make and use a composition comprising a nucleotide sequence encoding IL-2 and a nucleotide sequence encoding a MIP1β and a pharmaceutically acceptable carrier. One of ordinary skill in the art would have been motivated to combine the teachings because the composition and a pharmaceutically acceptable carrier well known to one of ordinary skill in the art for reducing tumors in an animal. Therefore, it would been obvious to one of ordinary skill in the art to make the composition with a pharmaceutically acceptable carrier.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicants' arguments filed 5/17/04 have been fully considered but they are not persuasive.

In response to applicants' arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants argue that Boursnell cites IL-2, MIPalpha and MIP1-beta along with more than 40 other immunomodulating polypetides and no motivation is provided to the skilled artisan to choose the combination as presently claimed. MPEP 2131.02 recites: "when the species is clearly named, the species claim is anticipated no matter how many other species are additionally named. Ex parte A, 17 USPQ2d 1716 (Bd. Pat. App. & Inter. 1990)." Furthermore, MPEP 2144.06 recites, "It is prima facie obvious to combine two compositions each of which is taught

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by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art. In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980)." This is the case here. At the time the invention was made, a vector comprising a nucleotide sequence encoding a MIP1β and a vector comprising a nucleotide sequence encoding IL-2 were known to treat a tumor in an animal. In addition, Boursnell taken with Hobart and LaFace and Song teaches the reasonable expectation of success for making a composition comprising a nucleotide sequence encoding multiple immunomodulating proteins. The argument with respect to MIP1-alpha is moot because MIP-alpha is not rejected under 103(a) and because this limitation is now deleted from the product claims.

Furthermore, the applicants are reminded that the motivation for combining the teachings of the prior art may be different from applicants' motivation to make the disclosed compositions. The fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). The office has provided motivation for making a composition comprising a nucleic acid sequence encoding MIP1β and a nucleotide sequence encoding IL-2.

Claims 1, 11, 13, 15, and 25-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boursnell et al. (US Patent 6,287,557) taken with Hobart et al. (US Patent 5,147,055) and LaFace (US 6,649,158) and Song et al., (J.Exp. Med., 186:1247-1256, 1997) in further view of Bruder et al. (US Patent 6,440,944).

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The rejection of the base claims 1, 11, 13, 15, and 26 under 35 U.S.C. 103(a) are applied here as indicated above, by Boursnell taken with Hobart and LaFace and Song. However, Boursnell taken with Hobart and LaFace and Song do not specifically teach making a replication defective adenoviral vector, wherein said adenoviral vector is deleted in the E1 region, or E1 and E4, or E1 and E3, or E1, E3, and E4.

However, at the time the invention was made, replication defective adenoviral vectors were well known to one of ordinary skill in the art for gene delivery because they are superior vehicles for transferring genetic material to a wide variety of cells and represent a safe choice of gene transfer. Bruder teaches that a variety of recombinant adenoviral vectors are known in the art for gene delivery (col. 1, lines 34-55). Bruder teaches an adenoviral vector with a gene of interest inserted into the E1 region of the adenovirus. Furthermore, Bruder teaches multiply deficient adenoviral vectors that are deficient in E1, E3 and E4. One of ordinary skill in the art understands that a recombinant adenoviral vector is replication defective because genes essential for adenovirus replication are deleted.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to make and use a replication defective adenoviral vector taught by Bruder in the composition taught by Boursnell taken with Hobart and LaFace and Song. One of ordinary skill in the art would have been motivated to use a replication defective adenoviral vector because they are superior vehicles for transferring genetic material to a wide variety of cells and represent a safe choice of gene transfer. In addition, one of ordinary skill in the art would have been motivated to use a multiply deficient adenoviral vector (E1-; E1-E4-; and E-1,

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E3-) to abolish expression of the adenoviral proteins (E1, E3, and/or E4) to improve the delivery of exogenous nucleic acid sequences to an animal.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicants' arguments filed 5/17/04 have been fully considered but they are not persuasive.

In response to applicants' arguments against the references individually (e.g., Bruder), one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). This is the case here. Bruder teaches that replication defective adenoviral vectors were well known in the art, at the time the invention was filed, for gene delivery because they are superior vehicle for transferring genetic material to a wide variety of cells and represent a safe choice of gene transfer. Thus, one skilled in the art would have been motivated to use a replication defective adenoviral vector in the claimed invention.

Claims 14, 15, 31, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boursnell et al. (US Patent 6,287,557) taken with Hobart et al. (US Patent 5,147,055) and LaFace (US 6,649,158) and Song et al., (J.Exp. Med., 186:1247-1256, 1997) in further view of Gruber (US Patent 6,410,326).

The rejection of the base claims 14, 15, and 31 under 35 U.S.C. 103(a) are applied here as indicated above, by Boursnell taken with Hobart and Song and LaFace. However, Boursnell

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taken with Hobart and LaFace and Song do not specifically teach making a poxvirus vector selected from the group consisting of vaccinia virus, MVA, and canary pox.

However, at the time the invention was made, vaccinia virus was well known to one of ordinary skill in the art for expressing heterologous proteins at high levels as taught by Gruber (col. 7, line 65, col.8, line 26).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to make and use vaccinia virus taught by Gruber in the composition taught by Boursnell taken with Hobart and LaFace and Song. One of ordinary skill in the art would have been motivated to make and use a vaccinia viral vector because vaccinia virus vectors were well known in the art for expressing heterologous proteins at high levels.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicants' arguments filed 5/17/04 have been fully considered but they are not persuasive.

In response to applicants' arguments against the references individually (e.g., Gruber), one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). This is the case here. A vaccinia virus was well known in the art for expressing heterologous proteins at high levels as taught by Gruber. Thus, one skilled in the art would have been motivated to use a vaccinia virus in the claimed invention.

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#### Conclusion

If a copy of a provisional application listed on the bottom portion of the accompanying Notice of References Cited (PTO-892) form is not included with this Office action and the PTO-892 has been annotated to indicate that the copy was not readily available, it is because the copy could not be readily obtained when the Office action was mailed. Should applicant desire a copy of such a provisional application, applicant should promptly request the copy from the Office of Public Records (OPR) in accordance with 37 CFR 1.14(a)(1)(iv), paying the required fee under 37 CFR 1.19(b)(1). If a copy is ordered from OPR, the shortened statutory period for reply to this Office action will not be reset under MPEP § 710.06 unless applicant can demonstrate a substantial delay by the Office in fulfilling the order for the copy of the provisional application. Where the applicant has been notified on the PTO-892 that a copy of the provisional application is not readily available, the provision of MPEP § 707.05(a) that a copy of the cited reference will be automatically furnished without charge does not apply.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, SPE - Art Unit 1635, can be reached at (571) 272-0760.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal

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Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Brian Whiteman Patent Examiner, Group 1635

SCOTT D. PRIEBE, PH.D PRIMARY EXAMINER

Sett D. Pruke

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